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Systems and Methods for Peripheral Nerve Stimulation as a Therapy for Chronic Pain

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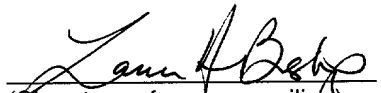
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Systems and Methods for Peripheral Nerve Stimulation as a Therapy for Chronic Pain

[0001] The present application claims the benefit of U.S. Provisional Patent Application Serial No. 60/265,009, filed January 30, 2001, which application is incorporated herein by reference in its entirety.

Field of the Invention

[0002] The present invention generally relates to implantable stimulator systems and methods, and more particularly relates to implantable stimulator systems and methods utilizing one or more implantable microstimulators for treating chronic pain with peripheral nerve stimulation.

Background of the Invention

[0003] Nociceptive pain is the signal of tissue irritation, impending injury, or actual injury. When nociceptors (i.e., pain receptors) in the affected area are activated, they transmit signals via the peripheral nerves and the spinal cord to the brain. Complex spinal reflexes (e.g., unconscious withdrawal of a hand from a hot surface) may be activated, followed by perception, cognitive and affective responses, and possibly voluntary action. The pain is typically perceived as related to the specific stimulus (e.g., hot, sharp) or with an aching or throbbing quality. Nociceptive pain is usually time-limited – although arthritis is a notable exception, and tends to respond well to treatment with opioids (e.g., morphine).

[0004] Visceral pain is a subtype of nociceptive pain. It tends to be paroxysmal and poorly localized, while somatic pain is more constant and well localized.

[0005] Neuropathic pain is the result of a malfunction somewhere in the nervous system. The site of the nervous system injury or malfunction can be either in the peripheral or in the central nervous system. The pain is often triggered by an injury, but this injury may not clearly involve the nervous system, and the pain may persist for months or years beyond the apparent healing of any damaged tissues. In this setting,

pain signals no longer represent ongoing or impending injury. Neuropathic pain frequently has burning, lancinating, or electric shock qualities. Persistent allodynia (i.e., pain resulting from a non-painful stimulus, such as light touch) is also a common characteristic of neuropathic pain. Neuropathic pain is frequently chronic, and tends to have a less robust response to treatment with opioids.

[0006] Pain is recognized as a major public health problem. It is estimated that chronic pain affects 15% to 33% of the U.S. population, or as many as 70 million people. In fact, chronic pain disables more people than cancer or heart disease and costs the American people more than both combined. Pain costs an estimated $70 billion a year in medical costs, lost working days, and workers' compensation.

[0007] The most common conditions associated with chronic neuropathic pain include:

[0008] Painful Peripheral Neuropathy (PN), including Diabetic Neuropathy (DN) and Traumatic Peripheral Nerve Injury: Many neuropathies have well-defined causes such as diabetes, peripheral vascular disease, uremia, AIDS, or nutritional deficiencies. Other causes include direct trauma; penetrating injuries; contusions; fractured or dislocated bones; mechanical pressure such as compression or entrapment; pressure involving the superficial nerves (ulna, radial, or common peroneal) which can result from a tumor or from prolonged use of crutches or staying in one position for too long; intraneural hemorrhage; exposure to cold or radiation; and vascular or collagen disorders such as atherosclerosis, systemic lupus erythematosus, scleroderma, sarcoidosis, rheumatoid arthritis, and polyarteritis nodosa. One example is phantom limb pain – a type of PN due to traumatic injury. These neuropathies usually start with numbness or tingling in the toes that slowly spreads upward, or occasionally starts in the fingers and moves up the hands. At times, symptoms may be barely noticeable, and at other times, especially at night, they may be almost unbearable. For some, symptoms are constant. Common symptoms include tingling, prickling or numbness; the sensation of wearing an invisible "glove" or "sock"; burning or freezing pain; sharp, jabbing or electric pain; extreme sensitivity to touch; muscle weakness; and loss of balance and coordination. PN

afflicts over 2 million Americans, most of whom are older adults. DN is a common complication of diabetes, affecting 60%-70% of diabetics.

[0009] Post-Herpetic Neuralgia (PHN): Herpes zoster, or "shingles", is an infection caused by the varicella-zoster virus, which is the virus that causes chickenpox. Shingles occurs in people who have had chickenpox and represents a reactivation of the dormant varicella-zoster virus. The virus typically causes a localized rash and associated pain, which usually go away within 3 to 5 weeks. But sometimes the pain continues long after the rash and blisters have cleared. This persistent pain is known as postherpetic neuralgia (PHN). PHN is the most common complication of shingles. It affects half of people over age 60 who develop shingles and 75 percent of people over age 70 with shingles. PHN results from damage to nerve fibers during shingles. Fibers that send messages from the skin to the brain send confused and exaggerated messages, thus causing pain. The pain takes different forms: sharp and jabbing, burning, or deep and aching. Extreme skin sensitivity may also be experienced, so that even the touch of clothing or a slight change in temperature produces severe pain. Some people also experience itching and numbness near the shingles site, even after the blisters have healed. Occasionally, the virus affects nerves that control muscle movement, causing muscle weakness, tremor or paralysis.

[0010] Reflex Sympathetic Dystrophy/Complex Regional Pain Syndrome (RSD/CRPS): The primary clinical feature of RSD/CRPS is pain in one or more extremities described as severe, constant, burning and/or deep aching pain. All tactile stimulation of the skin (e.g. wearing clothing, a light breeze) may be perceived as painful (allodynia). Other clinical features include skin changes (e.g., shiny, dry, or scaly) and swelling.

[0011] Fibromyalgia Syndrome (FMS): This is a disorder of unknown etiology affecting an estimated 2-4% of the general population, women more often than men. Patients complain that they ache all over. A large number of other symptoms are often present, particularly fatigue, morning stiffness, sleep disturbance, paresthesias, and headaches. On examination, areas of focal tenderness called tender points can be demonstrated in characteristic locations.

[0012] Another type of chronic pain, failed back surgery syndrome (FBSS), refers to patients who have undergone one or more surgical procedures and continue to experience pain. Included in this condition are recurring disc herniation, epidural scarring, and injured nerve roots.

[0013] Arachnoiditis, a disease that occurs when the membrane in direct contact with the spinal fluid becomes inflamed, causes chronic pain by pressing on the nerves. It is unclear what causes this condition.

[0014] Additional forms of chronic peripheral pain include, but are not limited to occipital neuralgia, peripheral pelvic pain, certain types of cardiac pain, and certain types of back pain. Many of these patients are treated symptomatically for their pain.

Brief Summary of the Invention

[0015] The invention disclosed and claimed herein provides means for chronically stimulating one or more peripheral nerves with a miniature implantable neurostimulator(s) that can be implanted with a minimal surgical procedure. To treat painful peripheral neuropathy and other forms of chronic peripheral pain, a miniature implantable neurostimulator, such as a Bionic Neuron (also referred to as a BION™ microstimulator), may be implanted via a minimal surgical procedure (e.g., injection or small incision) adjacent to one or more peripheral nerves. Nerves that may be stimulated by such a stimulator include, but are not limited to, one or more ulnar nerve, median nerve, radial nerve, common peroneal nerve, sciatic nerve, saphenous nerve, and intercostal nerves. A number of peripheral nerves, especially those in the extremities and in the thorax, lie relatively close to the surface of the skin and are surrounded by relatively few if any surgical barriers. A miniature neurostimulator may thus easily be implanted adjacent to a peripheral nerve.

[0016] A microstimulator may be implanted via injection and/or via endoscopic means. A more complicated surgical procedure may be required for sufficient access to a particular nerve (e.g., a deep nerve or a nerve surrounded by scar tissue) or for purposes of fixing the neurostimulator in place. A single microstimulator may be implanted, or two or more microstimulators may be implanted to achieve greater stimulation of one or more peripheral nerves. For instance, one or more

microstimulator(s) may be implanted adjacent to one or more of the greater occipital nerve, the lesser occipital nerve, and the third occipital nerve for the treatment of occipital neuralgia.

[0017] The microstimulator used with the present invention possesses one or more of the following properties, among others:

[0018] at least two electrodes for applying stimulating current to surrounding tissue;

[0019] electronic and/or mechanical components encapsulated in a hermetic package made from biocompatible material(s);

[0020] an electrical coil or other means of receiving energy and/or information inside the package, which receives power and/or data by inductive or radio-frequency (RF) coupling to a transmitting coil placed outside the body, thus avoiding the need for electrical leads to connect devices to a central implanted or external controller;

[0021] means for receiving and/or transmitting signals via telemetry;

[0022] means for receiving and/or storing electrical power within the microstimulator; and

[0023] a form factor making the microstimulator implantable via a minimal surgical procedure.

[0024] A microstimulator may operate independently, or in a coordinated manner with other implanted devices, or with external devices. For instance, a microstimulator may incorporate means for sensing pain, which it may then use to control stimulation parameters in a closed loop manner. The sensing and stimulating means may be incorporated into a single microstimulator, or a sensing means may communicate sensed information to at least one microstimulator with stimulating means.

Brief Description of the Drawings

[0025] The above and other aspects of the present invention will be more apparent from the following more particular description thereof, presented in conjunction with the following drawings wherein:

[0026] FIG. 1 illustrates an anterior view of the arteries and nerves of the right upper limb;

[0027] FIG. 2A is a posterior view of a dissection of the right leg, depicting various nerves, muscles, and bones of the lower limb;

[0028] FIG. 2B is an anterior view of a dissection of the right leg, depicting various superficial nerves and veins of the lower limb;

[0029] FIG. 3A is an anterior view of a dissection of the thoracic wall, depicting various nerves, muscles, and bones;

[0030] FIG. 3B is a cross-sectional view of a portion of the thorax, depicting various thoracic nerves, muscles, and bones;

[0031] FIG. 3C is an anterior view of a dissection of the back and head, depicting various nerves and muscles of the back and head;

[0032] FIG. 4 illustrates an exemplary embodiment of a stimulation system of the present invention;

[0033] FIG. 5 illustrates exemplary external components of the invention; and

[0034] FIG. 6 depicts a system of implantable devices that communicate with each other and/or with external control/programming devices.

[0035] Corresponding reference characters indicate corresponding components throughout the several views of the drawings.

Detailed Description of the Invention

[0036] The following description is of the best mode presently contemplated for carrying out the invention. This description is not to be taken in a limiting sense, but is made merely for the purpose of describing the general principles of the invention. The scope of the invention should be determined with reference to the claims.

[0037] Neuropathic pain is often poorly controlled by medication. Patients with refractory chronic peripheral pain have very few treatment alternatives. Surgery is often

ineffective, as the pain may return even when pain fibers are severed. Commercially available medication pumps allow continuous infusion of medication, and some may preferentially deliver medication to a local site of pain. Refractory chronic peripheral pain may also be controlled through the use of a transcutaneous electrical nerve stimulation (TENS) system or a spinal cord stimulation (SCS) system. These systems take advantage of the gate control theory of pain to mask local pain sensations with a tingling sensation.

[0038] All of these systems have drawbacks. Many are large devices that must apply stimulation transcutaneously. For instance, TENS is used to modulate the stimulus transmissions by which pain is felt by applying low-voltage electrical stimulation to large peripheral nerve fibers via electrodes placed on the skin. TENS devices can produce significant discomfort and can only be used intermittently.

[0039] Other devices require that a needle electrode(s) be inserted through the skin during stimulation sessions. These devices may only be used acutely, and may cause significant discomfort.

[0040] Implantable, chronic stimulation devices are available, but these currently require a significant surgical procedure for implantation. Surgically implanted stimulators, such as SCS systems, have been described in the art. These stimulators have different forms, but are usually comprised of an implantable control module (i.e., IPG) to which is connected to a series of leads that must be routed to nerve bundles in the spinal cord, to nerve roots and/or spinal nerves emanating from the spinal cord, or to peripheral nerves. The implantable devices are relatively large and expensive. In addition, they require significant surgical procedures for placement of electrodes, leads, and IPG. These devices may also require an external apparatus that needs to be strapped or otherwise affixed to the skin. Drawbacks, such as size (of internal and/or external components), discomfort, inconvenience, complex surgical procedures, and/or only acute or intermittent use has generally confined their use to patients with severe symptoms and the capacity to finance the surgery.

[0041] Significant research has been performed over the past 30 years evaluating the use of peripheral nerve stimulation for the management of refractory chronic peripheral pain. Circumferential electrodes treating mononeuropathies (i.e., a

nerve disease affecting only a single nerve) have given way to paddle electrode techniques and, most recently, the application of percutaneous wire electrode methods for minimally invasive peripheral nerve stimulation. Implantable chronic stimulation devices are available, but these suffer from the drawbacks described above. Recently, alternatives to 1) TENS, 2) percutaneous stimulation, and 3) bulky implantable stimulation assemblies have been introduced. Small, implantable microstimulators can be injected into soft tissues through a cannula or needle. See, e.g., U.S. Patent Numbers 5,324,316 and 5,405,367, both of which patents are incorporated herein by reference. Discussed herein are ways to effectively use such small, fully implantable, chronic neurostimulators for treating chronic peripheral pain.

[0042] FIG. 1 is an anterior view of arteries and nerves of the right arm. FIGS. 2A and 2B depict various nerves and muscles of the right leg. FIGS. 3A, 3B, and 3C show various nerves, muscles, and bones of the thorax, back, and head.

[0043] Among the most common complaints of painful peripheral neuropathy and other forms of chronic peripheral pain is pain in the limbs. As depicted in FIGS. 1, 2A and 2B, many nerves of the upper and lower limbs lie relatively close to the surface of the skin and are surrounded by relatively few, if any, surgical barriers. Examples of such peripheral nerves in the upper limbs (as depicted in FIG. 1) include the ulnar nerve 100, branches of the ulnar nerve 101, the musculocutaneous nerve 104, branches of the musculocutaneous nerve 105, the median nerve 106, branches of the median nerve 107, the radial nerve 110, branches of the radial nerve 111, the medial cutaneous nerve 112, and the intercostobrachial nerve 114. Examples of such peripheral nerves in the lower limbs (as depicted in FIGS. 2A and 2B) include the tibial nerve 116, branches of the tibial nerve 117, the common peroneal (or fibular) nerve 120, branches of the common peroneal nerve 121, the posterior cutaneous nerve 122, branches of the posterior cutaneous nerve 123, the sciatic nerve 126, branches of the sciatic nerve 127, the sural nerve 128, branches of the sural nerve 129, the saphenous nerve 130, and branches of the saphenous nerve 131. Others, not depicted, include the obturator nerve, the femoral nerve, the lateral cutaneous nerve, and their branches. In accordance with the teachings of the present invention, electrical stimulation at one or

more of the above and/or other peripheral nerves is relatively easy, and is provided to relieve peripheral pain.

[0044] Chronic pain may also be relieved with stimulation additionally or alternatively applied to nerves in the thorax, back, and head, as well as other peripheral nerves. As seen in FIGS. 3A, 3B, and 3C, many of these nerves also lie relatively close to the surface of the skin and are surgically accessible. Examples of such peripheral nerves include the intercostal nerves 136, branches of the intercostal nerves 138, the greater occipital nerve 140, the lesser occipital nerve 142, and the third occipital nerve 144. In accordance with additional teachings of the present invention, stimulation of, for instance, one or more of these nerves is alternatively or additionally provided to relieve peripheral pain.

[0045] Under normal conditions, pain signals are carried from the source of the pain through afferent nerve fibers which convey the impulses toward a nerve center (e.g., the brain or spinal cord). Pain signals are carried via nerve fibers toward the spinal cord, and are then conducted up an ascending nerve pathway to the brain, which processes the signals and induces the pain sensation. These pain signals travel through relatively small diameter nerve fibers (i.e., A-δ and C fibers), which are also relatively slow-conducting fibers.

[0046] Based on the gate control theory mentioned earlier, stimulating the fast-conducting, larger diameter nerve fibers (i.e., A-α and/or A-β fibers) will block, or gate, the slower pain signals from reaching the brain, or from being processed or recognized as pain signals. The somatic sensory fibers responsible for touch, pressure, and position sense are carried through these relatively large diameter nerve fibers. As such, relatively low amplitude stimulating current, which selectively activates these large diameter nerve fibers, may additionally or alternatively be applied to these peripheral nerve fibers as a treatment for chronic pain.

[0047] As indicated above, the present invention is directed to treating chronic pain using one or more small, implantable neurostimulators, referred to herein as "microstimulators". The microstimulators of the present invention are preferably, but not necessarily, similar to or of the type referred to as BION™ devices. The following documents describe various features and details associated with the manufacture,

operation, and use of BION implantable microstimulators, and are all incorporated herein by reference:

Application/Patent/ Publication No.	Filing/Publi-cation Date	Title
U.S. Patent 5,193,539	Issued Mar 16, 1993	Implantable Microstimulator
U.S. Patent 5,193,540	Issued Mar 16, 1993	Structure and Method of Manufacture of an Implantable Microstimulator
U.S. Patent 5,312,439	Issued May 17,1994	Implantable Device Having an Electrolytic Storage Electrode
U.S. Patent 5,324,316	Issued June 28, 1994	Implantable Microstimulator
U.S. Patent 5,405,367	Issued April 11, 1995	Structure and Method of Manufacture of an Implantable Microstimulator
U.S. Patent 6,051,017	Issued April 18, 2000	Improved Implantable Microstimulator and Systems Employing Same
PCT Publication WO 98/37926	published Sept 3, 1998	Battery-Powered Patient Implantable Device
PCT Publication WO 98/43700	published Oct 8, 1998	System of Implantable Devices For Monitoring and/or Affecting Body Parameters
PCT Publication WO 98/43701	published Oct 8, 1998	System of Implantable Devices For Monitoring and/or Affecting Body Parameters
	published Sept, 1997	Micromodular Implants to Provide Electrical Stimulation of Paralyzed Muscles and Limbs, by Cameron, et al., published in IEEE Transactions on Biomedical Engineering, Vol. 44, No. 9, pages 781-790.

[0048] As shown in FIG. 4, microstimulator device 150 includes a narrow, elongated capsule 152 containing electronic circuitry 154 connected to electrodes 156 and 158, which may pass through the walls of the capsule at either end. As detailed in the referenced patent publications, electrodes 156 and 158 generally comprise a stimulating electrode (to be placed close to the nerve) and an indifferent electrode (for completing the circuit). Other configurations of microstimulator device 150 are possible, as is evident from the above-referenced patent publications, and as described in more detail herein.

[0049] Certain configurations of implantable microstimulator 150 are sufficiently small to permit its placement adjacent to the structures to be stimulated. (As used herein, "adjacent" and "near" mean as close as reasonably possible to targeted tissue, including touching or even being positioned within the tissue, but in general, may be as

far as about 150 mm from the target tissue.) A single microstimulator 150 may be implanted, or two or more microstimulators may be implanted to achieve greater stimulation of the targeted tissue, or for a longer period of time.

[0050] Capsule 152 of FIG. 4 may have a diameter of about 4-5 mm, or only about 3 mm, or even less than about 3 mm. Capsule 152 length may be about 25-35 mm, or only about 20-25 mm, or even less than about 20 mm. The shape of the microstimulator may be determined by the structure of the desired target, the surrounding area, and the method of implantation. A thin, elongated cylinder with electrodes at the ends, as shown in FIG. 4, is one possible configuration, but other shapes, such as spheres, disks, or helical structures, are possible, as are additional electrodes.

[0051] Microstimulator 150 may be implanted with a surgical insertion tool specially designed for the purpose, or may be injected (e.g., via a hypodermic needle). Alternatively, device 150 may be implanted via conventional surgical methods, or may be inserted using other endoscopic or laparoscopic techniques. A more complicated surgical procedure may be required for fixing the neurostimulator in place.

[0052] The external surfaces of stimulator 150 may advantageously be composed of biocompatible materials. Capsule 152 may be made of, for instance, glass, ceramic, or other material that provides a hermetic package that will exclude water vapor but permit passage of electromagnetic fields used to transmit data and/or power. Electrodes 156 and 158 may be made of a noble or refractory metal or compound, such as platinum, iridium, tantalum, titanium, titanium nitride, niobium, or alloys of any of these, in order to avoid corrosion or electrolysis which could damage the surrounding tissues and the device.

[0053] In certain embodiments of the instant invention, microstimulator 150 comprises two, leadless electrodes. However, either or both electrodes 156 and 158 may alternatively be located at the ends of short, flexible leads as described in U.S. Patent Application No. 09/624,130, filed 7/24/2000, which is incorporated herein by reference in its entirety. The use of such leads permits, among other things, electrical stimulation to be directed more locally to a specific nerve or nerve branch a short distance from the surgical fixation of the bulk of the implantable stimulator 150, while

allowing most elements of stimulator 150 to be located in a more surgically convenient site. This minimizes the distance traversed and the surgical planes crossed by the device and any lead(s). In most uses of this invention, the leads are no longer than about 150 mm.

[0054] Microstimulator 150 contains, when necessary and/or desired, electronic circuitry 154 for receiving data and/or power from outside the body by inductive, radio-frequency (RF), or other electromagnetic coupling. In a some embodiments, electronic circuitry 154 includes an inductive coil for receiving and transmitting RF data and/or power, an integrated circuit (IC) chip for decoding and storing stimulation parameters and generating stimulation pulses (either intermittent or continuous), and additional discrete electronic components required to complete the electronic circuit functions, e.g., capacitor(s), resistor(s), coil(s), and the like.

[0055] Neurostimulator 150 includes, when necessary and/or desired, a programmable memory 160 for storing a set(s) of data, stimulation, and control parameters. Among other things, memory 160 may allow stimulation and control parameters to be adjusted to settings that are safe and efficacious with minimal discomfort for each individual. Specific parameters may provide therapeutic advantages for various forms of pain. For instance, some patients may respond favorably to intermittent stimulation, while others may require continuous stimulation to alleviate their pain.

[0056] In addition, stimulation parameters may be chosen to target specific neural populations and to exclude others, or to increase neural activity in specific neural populations and to decrease neural activity in others. For example, relatively low frequency neurostimulation (i.e., less than about 100-150 Hz) typically has an excitatory effect on surrounding neural tissue, leading to increased neural activity, whereas relatively high frequency neurostimulation (i.e., greater than about 100-150 Hz) may have an inhibitory effect, leading to decreased neural activity. In addition, large diameter nerve fibers (e.g., A-α and/or A-β fibers) respond to relatively low amplitude electrical current pulses compared with small diameter fibers (e.g., A-δ and/or C fibers).

[0057] Some embodiments of implantable stimulator 150 also includes a power source and/or power storage device 162. Possible power options for a stimulation

device of the present invention, described in more detail below, include but are not limited to an external power source coupled to stimulator 150, e.g., via an RF link, a self-contained power source utilizing any suitable means of generation or storage of energy (e.g., a primary battery, a replenishable or rechargeable battery such as a lithium ion battery, an electrolytic capacitor, a super- or ultra-capacitor, or the like), and if the self-contained power source is replenishable or rechargeable, means of replenishing or recharging the power source (e.g., an RF link, an optical link, a thermal link, or other energy-coupling link).

[0058] According to certain embodiments of the invention, a microstimulator operates independently. According to various embodiments of the invention, a microstimulator operates in a coordinated manner with other microstimulator(s), other implanted device(s), or other device(s) external to the patient's body. For instance, a microstimulator may control or operate under the control of another implanted microstimulator(s), other implanted device(s), or other device(s) external to the patient's body. A microstimulator may communicate with other implanted microstimulators, other implanted devices, and/or devices external to a patient's body via, e.g., an RF link, an ultrasonic link, a thermal link, an optical link, or the like. Specifically, a microstimulator may communicate with an external remote control (e.g., patient and/or physician programmer) that is capable of sending commands and/or data to a microstimulator and that may also be capable of receiving commands and/or data from a microstimulator.

[0059] In certain embodiments, and as illustrated in FIG. 5, the patient 170 switches the implantable stimulator 150 on and off by use of controller 180, which may be handheld. Implantable stimulator 150 is operated by controller 180 by any of various means, including sensing the proximity of a permanent magnet located in controller 180, sensing RF transmissions from controller 180, or the like.

[0060] External components for programming and/or providing power to various embodiments of implantable stimulator 150 are also illustrated in FIG. 5. When communication with the implanted stimulator 150 is desired, patient 170 is positioned on or near external appliance 190, which appliance contains one or more inductive coils 192 or other means of communication (e.g., RF transmitter and receiver). External appliance 190 is connected to or is a part of external electronic circuitry appliance 200

which may receive power 202 from a conventional power source. External appliance 200 contains manual input means 208, e.g., a keypad, whereby the patient 170 or a caregiver 212 can request changes in the stimulation parameters produced during the normal operation of the implantable stimulator 150. In these embodiments, manual input means 208 includes various electro-mechanical switches and/or visual display devices that provide the patient and/or caregiver with information about the status and prior programming of the implantable stimulator 150.

[0061] Alternatively or additionally, external electronic appliance 200 is provided with an electronic interface means 216 for interacting with other computing means 218, such as by a serial interface cable or infrared link to a personal computer or to a telephone modem or the like. Such interface means 216 may permit a clinician to monitor the status of the implant and prescribe new stimulation parameters from a remote location.

[0062] The external appliance(s) may be embedded in a cushion, pillow, mattress cover, or garment. Other possibilities exist, including a belt, patch, or other structure(s) that may be affixed to the patient's body or clothing. External appliances may include a package that can be, e.g., worn on the belt, may include an extension to a transmission coil affixed to the body, e.g., with a velcro band or adhesive, or may be combinations of these or other structures able to perform the functions described herein.

[0063] In order to help determine the strength and/or duration of electrical stimulation required to produce the desired effect, in some embodiments, a patient's response to and/or need for treatment is sensed. For example, electrical activity of the brain (e.g., EEG), nerve activity (e.g., ENG), muscle activity (e.g., EMG), patient mobility (e.g., cumulative accelerometer activity), sympathetic discharge, levels or changes in levels of medication, and/or endorphin level may be sensed. Other measures of the state of the patient may additionally or alternatively be sensed. For instance, neurotransmitter, hormone, cytokine, neuropeptide, and/or enzyme levels or their changes, and/or levels or changes in other substance(s) borne in the blood and/or in the cerebrospinal fluid (CSF) may be sensed, using, e.g., one or more Chemically Sensitive Field-Effect Transistors (CHEMFETs) such as Enzyme-Selective Field-Effect

Transistors (ENFETs) or Ion-Sensitive Field-Effect Transistors (ISFETs, as are available from Sentron CMT of Enschede, The Netherlands).

[0064] For example, when electrodes of implantable stimulator 150 are implanted adjacent to a peripheral nerve, a sensor or stimulating electrode (or other electrode) of microstimulator 150 may be used to sense changes in ENG resulting from the stimulation applied to the nerve. Alternatively, a "microstimulator" dedicated to sensory processes communicates with a microstimulator that provides the stimulation pulses. The implant circuitry 154 may, if necessary, amplify and transmit these sensed signals, which may be analog or digital. Other methods of determining the required stimulation include a sensor on one or more of the sympathetic ganglia for sensing increased sympathetic discharge and other markers of the potential for pain, a sensor implanted in the brain in an area where altered activity correlates with possible pain (e.g., the sensory thalamus), as well as other methods mentioned herein, and yet others that will be evident to those of skill in the art upon review of the present disclosure. The sensed information may be used to control stimulation parameters in a closed-loop manner.

[0065] For instance, in several embodiments of the present invention, a first and second "stimulator" are provided. The second "stimulator" periodically (e.g. once per minute) records a level of neural activity (or endorphin level, or cumulative accelerometer activity, etc.), which it transmits to the first stimulator. The first stimulator uses the sensed information to adjust stimulation parameters according to an algorithm programmed, e.g., by a physician. For example, the amplitude of stimulation may be increased in response to increased activity in nerves, nerve fibers, or brain areas which demonstrate increased activity during pain. In some alternatives, one stimulator performs both the sensing and stimulating functions, as discussed in more detail presently.

[0066] While a microstimulator may also incorporate means of sensing pain, it may alternatively or additionally be desirable to use a separate or specialized implantable device to record and telemeter physiological conditions/responses in order to adjust stimulation parameters. This information may be transmitted to an external device, such as external appliance 190, or may be transmitted directly to implanted

stimulator(s) 150. However, in some cases, it may not be necessary or desired to include a sensing function or device, in which case stimulation parameters are determined and refined, for instance, by patient feedback, or the like.

[0067] Thus, it is seen that in accordance with the present invention, one or more external appliances may be provided to interact with microstimulator 150, and may be used to accomplish, potentially among other things, one or more of the following functions:

[0068] Function 1: If necessary, transmit electrical power from the external electronic appliance 200 via appliance 190 to the implantable stimulator 150 in order to power the device and/or recharge the power source/storage device 162. External electronic appliance 200 may include an automatic algorithm that adjusts stimulation parameters automatically whenever the implantable stimulator(s) 150 is/are recharged.

[0069] Function 2: Transmit data from the external appliance 200 via the external appliance 190 to the implantable stimulator 150 in order to change the operational parameters (e.g., electrical stimulation parameters) used by stimulator 150.

[0070] Function 3: Transmit sensed data indicating a need for treatment or in response to stimulation from implantable stimulator 150 (e.g., EEG, ENG, EMG, endorphin level, or other activity) to external appliance 200 via external appliance 190.

[0071] Function 4: Transmit data indicating state of the implantable stimulator 150 (e.g., battery level, stimulation settings, etc.) to external appliance 200 via external appliance 190.

[0072] By way of example, a treatment modality for chronic upper extremity pain may be carried out according to the following sequence of procedures:

[0073] 1. A stimulator 150 is implanted so that its electrodes 156 and 158 are adjacent to the median nerve 106 of one or both arms, as needed. If necessary or desired, one or more additional stimulator(s) 150 may additionally or alternatively be implanted adjacent to other peripheral

nerves, such as the ulnar nerve(s) 100, the musculocutaneous nerve(s) 104, the radial nerve(s) 110, the medial cutaneous nerve(s) 112, the intercostobrachial nerve(s) 114, the axillary nerve(s) (not shown), branches of any of these nerves, or any portion of the brachial plexus.

[0074] 2. Using Function 2 described above (i.e., transmitting data) of external electronic appliance 200 and external appliance 190, implantable stimulator 150 is commanded to produce a series of electrical stimulation pulses with gradually increasing amplitude.

[0075] 3. After each stimulation pulse, series of pulses, or at some other predefined interval, any change in, e.g., ENG and/or endorphin or opiate level is sensed, for instance, by one or more electrodes 156 and 158 or sensors (e.g., a CHEMFET). These responses are converted to data and telemetered out to external electronic appliance 200 via Function 3.

[0076] 4. From the response data received at external appliance 200 from the implantable stimulator 150, or from other assessment, the stimulus threshold for obtaining a response is determined and is used by a clinician acting directly 212 or by other computing means 218 to transmit the desired stimulation parameters to the implantable stimulator 150 in accordance with Function 2.

[0077] 5. When patient 170 desires to invoke electrical stimulation to alleviate symptoms (e.g., pain, loss of function, etc.), patient 170 employs controller 180 to set the implantable stimulator 150 in a state where it delivers a prescribed stimulation pattern from a predetermined range of allowable stimulation patterns.

[0078] 6. To cease electrical stimulation, patient 170 employs controller 180 to turn off stimulator 150.

[0079] 7. Periodically, the patient or caregiver recharges the power source/storage device 162 of implantable stimulator 150, if necessary, in accordance with Function 1 described above (i.e., transmit electrical power).

[0080] For the treatment of any of the various types and degrees of chronic pain, it may be desirable to modify or adjust the algorithmic functions performed by the implanted and/or external components, as well as the surgical approaches, in ways that would be obvious to skilled practitioners of these arts. For example, in some situations, it may be desirable to employ more than one implantable stimulator 150, each of which could be separately controlled by means of a digital address. Multiple channels and/or multiple patterns of stimulation might thereby be programmed by the clinician and controlled by the patient in order to, for instance, deal with bilateral, complex, or multidimensional pain such as may occur as a result of peripheral neuropathy due to peripheral vascular disease, injury to multiple nerves, spinal cord injury, and/or failed back surgery syndrome (FBSS), for example.

[0081] In some embodiments discussed earlier, microstimulator 150, or a group of two or more microstimulators, is controlled via closed-loop operation. A need for and/or response to stimulation is sensed via microstimulator 150, or by an additional microstimulator (which may or may not be dedicated to the sensing function), or by another implanted or external device. If necessary, the sensed information is transmitted to microstimulator 150. In some embodiments, the stimulation parameters used by microstimulator 150 are automatically adjusted based on the sensed information. Thus, the stimulation parameters are adjusted in a closed-loop manner to provide stimulation tailored to the need for and/or response to stimulation.

[0082] For instance, in some embodiments of the present invention, a first and second "stimulator" are provided. The second "stimulator" periodically (e.g. once per minute) records a level of, e.g., nerve activity (ENG) and/or muscle activity (EMG), which it transmits to the first stimulator. The first stimulator uses the sensed information to adjust stimulation parameters according to an algorithm programmed, e.g., by a clinician. For example, stimulation amplitude may be increased in response to increased nerve and/or muscle activity. Alternatively, one "microstimulator" performs both the sensing and stimulating functions.

[0083] For example, as shown in the example of FIG. 6, a first microstimulator 150, implanted beneath the skin of patient 170, provides electrical

stimulation via electrodes 156 and 158 to a first location; a second microstimulator 150' provides electrical stimulation to a second location; and a third microstimulator 150" provides electrical stimulation to a third location. As mentioned earlier, the implanted devices may operate independently or may operate in a coordinated manner with other similar implanted devices, other implanted devices, or other devices external to the patient's body, as shown by the control lines 222, 223 and 224 in FIG. 6. That is, in accordance with certain embodiments of the invention, external controller 220 controls the operation of each of the implanted microstimulators 150, 150' and 150".

[0084] According to various embodiments of the invention, an implanted device, e.g. microstimulator 150, may control or operate under the control of another implanted device(s), e.g., microstimulator 150' and/or microstimulator 150". That is, a device made in accordance with the invention may communicate with other implanted stimulators, other implanted devices, and/or devices external to a patient's body, e.g., via an RF link, an ultrasonic link, a thermal link, an optical link, or other communications link. Specifically, as illustrated in FIG. 6, microstimulator 150, 150', and/or 150", made in accordance with the invention, may communicate with an external remote control (e.g., patient and/or physician programmer 220) that is capable of sending commands and/or data to implanted devices and that may also be capable of receiving commands and/or data from implanted devices.

[0085] A microstimulator made in accordance with the invention may incorporate, in some embodiments, first sensing means 228 for sensing therapeutic effects, clinical variables, or other indicators of the state of the patient, such as ENG, EEG, EMG, patient mobility, sympathetic discharge, and/or other marker of the potential for pain. The stimulator additionally or alternatively incorporates second means 229 for sensing levels or changes in one or more medications, neurotransmitters, hormones, cytokines, neuropeptides, endorphins, enzymes, and/or other substances in the blood plasma, in the cerebrospinal fluid, or in the local interstitial fluid. The stimulator additionally or alternatively incorporates third means 230 for sensing electrical current levels and/or waveforms supplied by another source of electrical energy. Sensed information may be used to control the parameters of the stimulator(s) in a closed loop manner, as shown by control lines 225, 226, and 227. Thus, the sensing means may be

incorporated into a device that also includes electrical stimulation means, or the sensing means (that may or may not have stimulating means) may communicate the sensed information to another device(s) with stimulating means.

[0086] While a microstimulator may also incorporate means of sensing the condition of a patient, e.g., via ENG, EEG, EMG, or patient mobility, it may alternatively or additionally be desirable to use a separate or specialized implantable device to sense and telemeter physiological conditions/responses in order to adjust stimulation parameters. This information may be transmitted to an external device, such as external appliance 220, or may be transmitted directly to implanted stimulator(s) 150. However, in some cases, it may not be necessary or desired to include a sensing function or device, in which case stimulation parameters may be determined and refined, for instance, by patient feedback.

[0087] As mentioned earlier, large diameter fibers (e.g., A-α and A-β fibers) respond to relatively lower current density stimulation vis-á-vis small diameter fibers (e.g., A-δ and C fibers). These smaller A-δ and C fibers are generally responsible for carrying pain and temperature signals, while the A-α and A-β fibers generally carry pressure, light touch, and proprioceptive information. Therefore, pain may be masked, decreased or otherwise controlled or removed by activating the larger A-α and/or A-β fibers, so the signals from the A-δ and/or C fibers are "masked," or "gated."

[0088] For example, microstimulator(s) 150 may be implanted adjacent to one or more peripheral nerves in one or both legs (e.g., the common peroneal nerve(s) 120, sciatic nerve(s) 126, saphenous nerve(s) 130, branches/divisions of these nerves, and/or other peripheral nerves in the legs) to treat peripheral neuropathy in a patient's leg(s) (see FIGS. 2A and 2B). In some embodiments of the invention, the microstimulator(s) are programmed to provide relatively low-current stimulation pulses (e.g., at less than about 1-10 mA, depending on proximity of the stimulator to the target neural tissue), which is likely to cause the sensation of pressure, light touch, proprioceptive, and other non-nociceptive sensations. These sensations may be sufficient to mask, block, or otherwise attenuate or control the pain signals.

[0089] If, instead or additionally, the peripheral neuropathy is located in one of the patient's arms, this relatively low amplitude stimulation applied to one or more

peripheral nerve fibers in the arm (e.g. the ulnar nerve 100, median nerve 106, radial nerve 110, branches/divisions of these nerves, and/or other peripheral nerves in the arm) may provide relief. As mentioned earlier, one or more of at least the greater occipital nerve 140, the lesser occipital nerve 142, and the third occipital nerve 144 may be stimulated for relief from, e.g., occipital neuralgia.

[0090] Chronic pain in the thorax or other areas (e.g. the arm, back or abdomen) may best be relieved with relatively low amplitude stimulation of one or more peripheral nerve fibers in the thorax (e.g. one or more intercostal nerves 136, branches/divisions of intercostal nerves, and/or other peripheral nerves in the thorax). For instance, intercostal pain due to postherpetic neuralgia may be relieved with stimulation of an affected intercostal nerve, which stimulation may also treat certain types of back and/or cardiac pain.

[0091] According to several embodiments of the invention, pain is alleviated by additionally or alternatively increasing excitement of these nerve fibers. Relatively low-frequency electrical stimulation (e.g., less than about 100-150 Hz) is likely to produce such excitement. This low-amplitude, low-frequency therapy is most likely to provide relief to patients with peripheral neuropathy, among other problems.

[0092] Additionally, sensing means described earlier may be used to orchestrate first the activation of microstimulator(s) targeting one or more nerves to control pain in one area, and then, when appropriate, the microstimulator(s) targeting nerves that control pain in another area and/or by a different means. Alternatively, this orchestration may be programmed, and not based on a sensed condition.

[0093] While the invention herein disclosed has been described by means of specific embodiments and applications thereof, numerous modifications and variations could be made thereto by those skilled in the art without departing from the scope of the invention set forth in the claims.